Risk and Protective Factors for Suicide Among Patients With Methamphetamine Dependence: A Nested Case-Control Study

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Objective: Methamphetamine as a recreational drug has undergone cycles of popularity, with a recent surge worldwide since the 1990s. This study aimed to identify clinical characteristics associated with suicide mortality in patients with methamphetamine dependence by means of a nested case-control design.

Method: In a consecutive series of 1,480 inpatients with methamphetamine dependence (diagnosed according to *DSM-III-R* and *DSM-IV* criteria) admitted to a psychiatric center in northern Taiwan from January 1, 1990, through December 31, 2006, 38 deaths due to suicide were identified as cases via record linkage, and 76 controls were randomly selected using risk-set density sampling in a 2:1 ratio, matched for age, sex, and the year of index admission. A standardized chart review process was adopted to collate sociodemographic and clinical information for each study subject. Multivariate conditional logistic regression analysis was used to identify correlates of suicide among these patients.

Results: For the sociodemographic and symptom profiles at the latest admission, financial independence lowered the risk for suicide (adjusted risk ratio [ARR] = 0.33, $P < .05$), whereas visual hallucinations elevated the risk (ARR = 2.57, $P < .05$) for suicide. For the profiles during the postdischarge period, financial independence (ARR = 0.11, $P < .05$) remained associated with reduced risk for suicide, whereas suicide attempt (ARR = 8.78, $P < .05$) and depressive syndrome (ARR = 3.28, $P = .059$) were associated with increased risk of suicide.

Conclusions: Both protective and risk factors for suicide mortality were found among inpatients with methamphetamine dependence, and the findings have implications for clinical intervention and prevention.

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Methamphetamine is a synthetic central nervous system stimulant that acts by increasing the synaptic concentration of monoamine neurotransmitters in the brain.[1] Ever since its introduction as an anorectic in the 1920s, methamphetamine has undergone cycles of popularity as a recreational drug worldwide. Since the 1990s, the renewed popularity of methamphetamine hydrochloride is attributable to a new dosage form (a pure crystal called "ice") and an inhalable route of administration; it has been accompanied by growth of makeshift chemical laboratories to manufacture the crystal methamphetamine.[2] The abuse of methamphetamine has become one of the fastest-growing illicit drug problems worldwide, particularly in Southeast Asia, Australia, and North America.[3] Long-term use of methamphetamine results in physical and mental consequences, including intermingling of mood changes and psychosis[4,5]; suicide is one of the most serious consequences of methamphetamine abuse.[6,7] A recent study[7] in the United States reported that 29% of methamphetamine-dependent patients had attempted suicide during their lifetime.

As a stimulant of the central nervous system, methamphetamine is similar to cocaine in its potent sympathomimetic and euphoriant activities. However, chronic use of methamphetamine is more likely than cocaine to induce psychotic symptoms[8] that closely resemble those of paranoid schizophrenia, and the symptoms may vary with the course of methamphetamine dependence.[9,10] Furthermore, schizophrenia shares a familial predisposition with schizotypal personality disorder that reflects the liability to schizophrenia.[11] The premorbid schizotypal personality also might predispose methamphetamine users to develop psychosis, and the persistence of the psychosis is correlated with increased presence of these personality features.[10] Despite the fact that methamphetamine use disorder and schizophrenia are different disease entities, these two share similar psychotic symptom profiles and underlying premorbid personality types. These findings suggest that methamphetamine use may induce suicide via a mechanism similar to that of schizophrenia.

The enormous body of literature on the risk factors for suicide in schizophrenia may help shed light on the corresponding risk factors for suicide in methamphetamine-dependent individuals. A meta-analysis[12] found that the major risk factors for suicide among patients with schizophrenia included depression, previous suicide attempts, drug misuse, agitation, and recent loss, whereas existence of hallucinations was associated with a reduced risk of suicide. Unemployment or low income, which was associated with increased risk of suicide in the general population,[13,14] was not associated with suicide in patients with schizophrenia.[12] However, patients with methamphetamine dependence might differ from patients with schizophrenia in this aspect since the former tend to be under persistent financial pressure to satisfy their drug craving. Whether methamphetamine dependence shares similar risk factors for suicide mortality with schizophrenia remains to be clarified.

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In general, suicide mortality is relatively rare during a short-term period.[15] Instead, a few cross-sectional studies[16,17] explored factors associated with suicidal ideation, and another follow-up study[7] examined such factors associated with suicide attempts in methamphetamine users. None of them directly addressed the issue of suicide mortality among methamphetamine users.

Under these circumstances, a case-control study with a sufficient number of suicidal deaths ascertained from a cohort under a long period of follow-up is a relatively feasible approach to determine risk factors for methamphetamine-related suicide mortality. The difficulty in maintaining contact with methamphetamine-dependent patients to assess the outcome of suicide mortality could be overcome by the process of data linkage with other sources.[18] To fill the gap in the literature, we set out to conduct a sex- and age-matched nested case-control study on the basis of a cohort of inpatients with methamphetamine dependence. The aim of the study was to identify potential clinical factors associated with suicide mortality in these patients, including psychopathological symptoms during acute hospitalization and the postdischarge stage.

METHOD

Study Population

A consecutive series of 1,480 inpatients with methamphetamine dependence who were admitted to Taipei City Psychiatric Center, which is designated as a psychiatric service center for northern Taiwan, from January 1, 1990, through December 31, 2006, were enrolled as the retrospective cohort for this study. The inclusion criterion for the study was a principal psychiatric diagnosis of methamphetamine dependence according to the criteria of the *Diagnostic and Statistical Manual of Mental Disorders*, Third Edition, Revised (*DSM-III-R*), and Fourth Edition (*DSM-IV*).[19,20] We retrieved the discharge diagnosis routinely made by a senior in-charge board-certified psychiatrist who had reviewed several types of clinical information on each inpatient during each admission, including that of a comprehensive evaluation by a multidisciplinary team and a positive urine test for methamphetamine use shortly before hospitalization. Exclusion criteria were a history of psychosis before methamphetamine use and a possible relationship between psychotic symptoms and psychedelic substance or substances other than methamphetamine. Opportunistic methamphetamine users, those who had used the drug less than 20 times in the past year, were also excluded.[21] All of the board-certified psychiatrists who participated in this study received their residency training at Taipei City Psychiatric Center and demonstrated satisfactory reliability in making psychiatric diagnoses.[22] This study was approved by the Institutional Review Board of the Committee on Human Subjects of Taipei City Hospital, Taipei, Taiwan.

Case Ascertainment and Control Selection

The unique national identification number for each citizen in Taiwan was used as an identifier in the linking process to search for deceased subjects. Each cohort member was electronically linked against databases from the Death Certification System of the Taiwan Department of Health issued from January 1, 1990, through December 31, 2006, and 127 deaths were identified. Of these, 79 were unnatural deaths and 48 were natural deaths. Of the unnatural deaths, 41 were suicides, and the rest were either accidental deaths (n = 25) or of undetermined cause (n = 13). The mean crude total mortality and suicide rates for the cohort were 1,336/100,000 and 427/100,000 per year, respectively, which were higher than those of the general population in Taiwan, with mean rates of 557/100,000 and 11/100,000 per year, respectively, from 1990 to 2006.[23] For suicide, based on the new World Health Organization standard population[24] with direct standardization, the age-adjusted suicide rate of the cohort was 670/100,000, which was significantly higher than that of the general population of Taiwan (10/100,000).

If a patient had multiple hospitalizations during the study period, the earliest one was defined as the index admission. Using the deceased subjects as cases, we conducted a nested case-control study among the cohort (n = 1,480) using risk-set sampling (ie, incidence density sampling) for controls. To obtain an unbiased estimate of the risk ratio, controls were selected randomly from subjects who were alive at the time of death of each new case in a 2:1 ratio matched for age (± 5 years), sex, and the year of index admission. Cases that were identified later during the follow-up were eligible to serve as controls for earlier cases. During the study period, 2 subjects were first selected as controls and later became cases, while another 2 controls were selected twice for the analysis.

To investigate the effect of methamphetamine use without being confounded by other substances, we excluded any patients whose principal psychiatric diagnosis after the index admission was changed to one other than methamphetamine use disorder (n = 3). A total of 38 pairs of case-control units (ie, 38 cases and 76 controls) were included in this study. Among the 114 subjects, 29 had multiple hospitalizations, but the proportion did not differ between cases and controls.

Data Collection

The methodology used to collate clinical information in this study is described in more detail elsewhere[25] and is briefly summarized here. Semistructured case notes were used for any inpatient who was admitted to Taipei City Psychiatric Center since 1980. The form used in collecting this information contained over 95 items covering sociodemographics and the detailed psychiatric evaluation (eg, history of substance use, mental status examination, physical condition, and family history). A parallel interview to confirm the information with family members or others who knew the patient well was routinely conducted during the admission. On the first morning after admission, a fasting venous blood sample was routinely drawn for biochemical analyses.

Information for each subject was carefully checked using a combined review process by a trained clinical psychologist (C.L.C.) and then double-checked by 1 of 3 psychiatrists, including a senior psychiatrist (C.J.K.) and 2 trained psychiatric

residents with 2 years of clinical practice. The chart reviewers were blinded to the subjects' case or control status. To facilitate the chart review, a structured abstraction form containing 125 items was developed that typically required about 1 hour to complete, including information on demographics, social support network, substance use history, laboratory data relating to the index and latest hospital admissions and other clinical features, and the symptom profiles at the index admission and the latest admission, as well as the postdischarge period from the latest admission. After discharge, the subjects remained under intensive follow-up at outpatient services, where periodic urine screening is requested. On the basis of follow-up information, almost none of the participants showed any sign of methamphetamine use.

We adopted the same criteria used previously[25] for the diagnosis of depressive syndrome after discharge from the latest admission, requiring at least 1 of the following conditions: (1) prescription of any antidepressant, eg, selective serotonin reuptake inhibitors or tricyclic antidepressants, for the treatment of depression with clinical attention and (2) depressed mood plus at least 1 other symptom of major depressive episode (according to *DSM-IV*) recorded on the medical chart. Symptom profiles were rated on the basis of the most severe presentation of each item during the specified period, and only symptoms that received clinical attention were defined as being present. Suicide attempt was defined as any serious, potentially life-threatening act that was not self-mutilating in nature. An act that was listed in medical records either as not lethal or as a trivial injury associated with attention-calling toward others was not considered a suicide attempt.

Before the review process, all of the chart reviewers participated in a reliability study and rated information independently for 4 cases and 8 controls. The results showed satisfactory interrater reliability, with κ values of key variables all greater than 0.7, including symptom profiles, depressive syndrome, and comorbid schizophrenia or other substance use disorders.

Statistical Analyses

Initial comparisons between cases and controls were performed using univariate conditional logistic regression analyses. Then multivariate conditional logistic regression analyses were conducted by means of a backward variable selection procedure using the PROC PHREG of SAS software, version 9.1 (SAS Institute Inc; Cary, North Carolina). Variables with at least a moderate association with suicide ($P < .20$) were included in the final multivariate model. Depending on the psychiatric status at different time points during the illness course, 2 explanatory models were used, including symptom profiles at acute hospitalizations and those at the recovery stage.

The magnitude of each risk factor's contribution to suicide among patients with methamphetamine dependence was estimated using the attributable fraction method among the exposed with the following formula: (RR – 1)/RR, in which RR is the risk ratio estimated by the multivariate conditional logistic regression analysis.[26] If the RR is less than 1, a protective fraction was derived, instead, as 1 – RR.

Table 1. Sociodemographic Characteristics of Suicide Completers and Living Controls Among Patients With Methamphetamine Dependence (N = 114)

Characteristic	Suicide Completers (n = 38)	Living Controls (n = 76)	Risk Ratio[a]	95% CI
Sex, male, n (%)	31 (81.6)	62 (81.6)	…	…
Age, mean (SD), y[b]	28.8 (6.6)	28.9 (7.0)	0.99	0.90–1.09
Age at first methamphetamine use, mean (SD), y[b]	22.3 (6.7)	22.4 (6.9)	0.98	0.92–1.04
Married, n (%)[b]	5 (13.2)	13 (17.1)	0.73	0.23–2.24
Living with family, n (%)[b]	32 (84.2)	62 (81.6)	1.23	0.41–3.71
Education ≥ 12 years, n (%)[b]	11 (28.9)	33 (43.4)	0.56	0.25–1.24
Employment, n (%)				
Lifetime	31 (81.6)	62 (81.6)	1.00	0.37–2.74
Index admission	8 (21.1)	21 (27.6)	0.71	0.29–1.76
Latest admission	6 (15.8)	16 (21.1)	0.69	0.24–2.01
Financial independence, n (%)				
Index admission	10 (26.3)	36 (47.4)	0.38*	0.15–0.93
Latest admission	7 (18.4)	33 (43.4)	0.30*	0.12–0.78
Hollingshead Socioeconomic Status, class IV or V, n (%)				
Index admission	36 (94.7)	68 (89.5)	2.00	0.43–9.42
Latest admission	37 (97.4)	71 (93.4)	2.50	0.29–21.40

[a]Estimated using univariate conditional logistic regression.
[b]At index admission.
*$P < .05$.
Symbol: … = matched by design.

RESULTS

Demographics and Drug Use History

Both the suicide completers and the controls among the methamphetamine-dependent patients in this study had similar distributions of sex, age, age at first methamphetamine use, marital status, living with family, educational level, employment, and socioeconomic status according to the Hollingshead[27] classification (Table 1). The only difference between the 2 groups was that a lower proportion of cases had financial independence, ie, being able to economically support themselves without assistance, at both index and latest admissions.

Among the 38 suicide completers, the mean interval from the index admission to suicide was 3.8 (SD = 3.1) years, and the mean interval from the latest admission to suicide was 2.8 (SD = 3.0) years. The methods used by the suicide completers included drugs/poisons (n = 15), hanging (n = 7), jumping from a high place (n = 7), charcoal burning/other gases (n = 6), drowning (n = 1), and others (n = 2); none used firearms. There was no difference between the 2 groups in terms of family history of psychiatric disorders, including schizophrenia, substance use disorders, and suicide (data not shown).

Psychiatric Symptomatology at the Latest Admission and After Discharge

When the psychopathological symptoms at the index admission were compared between the cases and the controls, no difference was found. However, this was not the

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Table 2. Psychopathological Characteristics of Suicide Completers and Living Controls Among Inpatients With Methamphetamine Dependence at the Latest Admission and Postdischarge From the Latest Admission (N = 114)

Characteristic	Suicide Completers	Living Controls	Risk Ratio[a]	95% CI
At latest admission	(n = 38)	(n = 76)		
With psychosis, n (%)	26 (68.4)	55 (72.4)	0.83	0.36–1.92
Comorbidity, n (%)				
Substance/alcohol use disorders	8 (21.1)	14 (18.4)	1.23	0.42–3.66
Schizophrenia	10 (26.3)	11 (14.5)	2.60	0.84–8.04
Others	6 (15.8)	6 (7.9)	2.16	0.65–7.19
Psychosis-related symptoms, n (%)	34 (89.5)	58 (76.3)	2.33	0.77–7.01
Auditory hallucination	28 (73.7)	48 (63.2)	1.61	0.69–3.78
Visual hallucination	14 (36.8)	13 (17.1)	2.71*	1.11–6.22
Persecutory delusion	22 (57.9)	40 (52.6)	1.23	0.57–2.67
Reference delusion	21 (55.3)	30 (39.5)	1.93	0.86–4.36
Other psychotic symptoms	17 (68.4)	32 (55.3)	1.11	0.52–2.37
Suicide attempt, n (%)	13 (34.2)	12 (15.8)	3.49*	1.19–10.21
Discharged against medical advice, n (%)	11 (28.9)	25 (32.9)	0.81	0.32–2.01
Laboratory markers, mean (SD)				
Blood hemoglobin, g/dL	14.0 (1.9)	14.7 (1.5)	0.71*	0.51–1.00
Fasting blood sugar, mg/dL	86.2 (12.1)	87.2 (11.4)	0.99	0.95–1.03
Serum aspartate aminotransferase, U/L	39.8 (63.7)	27.4 (21.0)	1.01	0.99–1.03
Serum alanine aminotransferase, U/L	36.1 (47.3)	31.0 (34.3)	1.01	1.00–1.02
Serum cholesterol, mg/dL	166.0 (18.2)	175.6 (39.8)	1.00	0.98–1.01
Serum triglyceride, mg/dL	105.6 (47.7)	115.4 (73.7)	1.00	0.99–1.01
Postdischarge from latest admission[b]	(n = 29)	(n = 61)		
Depressive syndrome, n (%)	18 (62.1)	20 (32.8)	2.23+	0.92–5.40
Anxiety with clinical attention, n (%)	15 (51.7)	17 (27.9)	6.16*	1.31–29.04
Suicide attempt, n (%)	9 (31.0)	4 (6.6)	3.09**	1.12–8.56

[a]Estimated using univariate conditional logistic regression.
[b]Twenty-four subjects were lost to follow-up after the discharge.
+$P = .077$, *$P < .05$, **$P < .01$.

Table 3. Multivariate Conditional Logistic Regression of Risk Factors for Suicide Mortality Among Patients With Methamphetamine Dependence

Variable	Adjusted Risk Ratio	95% CI	*P* Value
Model 1 (based on the variables at latest admission)			
Financial independence	0.33	0.12–0.91	.032
Visual hallucination	2.57	1.01–6.52	.047
Suicide attempt	2.86	0.87–9.40	.084
Model 2 (based on the variables during the period after discharge from latest admission)			
Financial independence	0.11	0.02–0.70	.019
Depressive syndrome	3.28	0.96–11.26	.059
Suicide attempt	8.78	1.17–65.69	.034
Anxiety with clinical attention	2.94	0.75–11.55	.120

case at the latest admission; the symptom profiles of the latest admission episode are displayed in Table 2. Among the symptoms examined, the suicide completers had a greater prevalence of visual hallucinations and suicide attempt than the controls. Among the laboratory markers examined, suicide completers had a lower mean level of hemoglobin than the controls, while no difference between the 2 groups was found in the blood concentrations of fasting glucose, aspartate aminotransferase, alanine aminotransferase, cholesterol, and triglycerides.

Among the 114 subjects in this study, 24 were lost to outpatient follow-up, with no difference in the proportion between the 2 groups (9 cases and 15 controls). During the period after the discharge from the latest admission, the suicide completers had a greater prevalence of depressive syndrome and suicide attempts than the controls (lower part of Table 2).

The distributions of symptoms of major depressive episodes with a significant difference between cases and controls after the latest discharge (2 of 9 symptoms) included recurrent thoughts of death (34.5% vs 8.2%, respectively; $P = .05$) and significant weight/appetite change (41.4% vs 21.3%, respectively; $P = .04$). The other 7 nonsignificant symptoms (cases versus controls) included depressed mood (62.1% vs 32.8%; $P = .12$), markedly diminished interest (6.9% vs 1.6%; $P = .45$), sleep problems (82.8% vs 67.2%; $P = .10$), psychomotor agitation/retardation (3.4% vs 4.9%; $P = .61$), fatigue or loss of interest (6.9% vs 14.8%; $P = .60$), inability to concentrate (3.4% vs 9.8%; $P = .34$), and feelings of worthlessness (13.8% vs 0.0%; $P = .90$). The depression symptoms were highly correlated to depressive syndrome; therefore, they were not included in the multivariate analysis.

Furthermore, the prescription of any antidepressant in criterion 1 of depressive syndrome was coded as positive only among those who received an antidepressant for the treatment of depression rather than other clinical conditions, such as obsessive-compulsive symptoms. The prevalence of obsessive-compulsive symptoms with clinical attention was low after the latest discharge (1 of 90 subjects; 1.1%). None of the subjects was prescribed an antidepressant for treatment of obsessive-compulsive symptoms.

The relationships of visual hallucinations to the other 2 symptom correlates were then examined. Visual hallucination during the latest admission for methamphetamine dependence was associated (cases vs controls) with a higher proportion of postdischarge nonfatal attempted suicide (46.7% vs 9.7%; $\chi^2 = 7.11$, $P = .008$) but not with depressive syndrome (45.5% vs 41.2%; $\chi^2 = 0.12$, $P = .72$).

Multivariate Analysis

In conducting the multivariate conditional logistic regression analyses, sociodemographic and symptom profiles at 2 different time points were evaluated (Table 3). For the profiles at the latest admission (model 1), financial independence lowered the risk of suicide, whereas the presence of visual hallucinations elevated the risk for suicide. Meanwhile, for the profiles after discharge from the latest admission (model 2), financial independence remained associated with a reduced risk of suicide, whereas the presence of suicide attempt and depressive syndrome (with a marginal significance, $P = .059$) was associated with a substantially increased risk of suicide.

Attributable Fraction and Protective Fraction

Based on the risk ratio estimates derived from the conditional logistic regression analyses, the protective fraction of financial independence for the risk of suicide among patients with methamphetamine dependence was estimated

to be 67% (model 1) and 89% (model 2). The attributable fraction for visual hallucinations at the latest admission (model 1) for suicide was 61%, and, for suicide attempt, was 89%; the attributable fraction for depressive syndrome after discharge from the latest admission (model 2) was 70%.

DISCUSSION

To our knowledge, this is the first study to investigate the risk and protective factors for suicide mortality among patients with methamphetamine dependence. By means of a nested case-control study that is clear in temporal sequence and less confounded by recall bias, our results revealed that the presence of visual hallucinations during acute hospitalization and nonfatal suicide attempt and depressive syndrome during the postdischarge period are associated with an increased risk of suicide. On the other hand, financial independence was associated with a decreased risk of suicide. These findings have important implications for clinical intervention and prevention.

In this study, we retrieved detailed information on subjects' clinical symptomatology by means of a standardized chart review process. Nevertheless, the suicide mortality among these patients was associated only with symptoms at the latest hospital admission and not with those at the index admission. For example, the distribution of visual hallucinations differed significantly between cases and controls for the latest hospital admission (36.8% vs 17.1%, respectively; $P = .03$) but not the index admission (26.3% vs 17.1%, respectively; $P = .24$). This finding indicates that, even for patients with chronic methamphetamine use, clinical management during an acute exacerbation (ie, the need to be rehospitalized because of methamphetamine use) has important value in the prevention of patients' postdischarge suicide. It alerts the clinicians to follow up with the patients closely after discharge if the patients have multiple hospitalizations due to methamphetamine use.

Our finding that visual hallucinations during acute hospitalization for methamphetamine dependence is a risk factor for suicide contrasts with the results of a meta-analysis[12] of risk factors for suicide among patients with schizophrenia, in which hallucinations in schizophrenic patients were associated with a reduced risk of suicide. Since visual hallucinations during acute hospitalizations for methamphetamine dependence were associated with postdischarge nonfatal attempted suicides, but not with depressive syndrome, these patients' visual hallucinations may lead to suicide via a method independent of affect change. Whether the content of the hallucinations for amphetamine dependence differs from that for schizophrenia[28] warrants further investigation.

The association of postdischarge depressive syndrome with suicide mortality for patients with methamphetamine dependence in this study extends the finding from a previous study[7] on attempted suicide among methamphetamine users and is compatible with the findings from studies of schizophrenia.[12,25] It is noteworthy that this study used reliable information to avoid recall bias in defining depressive syndrome after the latest admission, ie, either the prescription of an antidepressant or depressed mood plus at least 1 other documented symptom (according to *DSM-IV*) of a major depressive episode. The severity of depressive syndrome approximates that of a mild depressive episode listed as F32.0 in the *International Classification of Diseases, Tenth Revision*,[29] instead of the *DSM-IV* criteria for a major depressive episode.[20] An important implication of our finding is that clinicians should be careful to screen for depressive symptoms during the follow-up of patients with methamphetamine dependence in the recovery stage, and they should be more aggressive in treating those who have significant clinical depression symptoms, particularly those relating to recurrent thoughts of death and significant weight/appetite change, in order to prevent suicide. Since medications for the treatment of methamphetamine dependence are emerging,[30] further study on the efficacy of antidepressants among methamphetamine users with depressive syndrome during the recovery stage is warranted.

Our finding that attempted suicide during either acute hospitalization or the postdischarge period was a risk factor for suicide mortality is consistent with previous studies in patients with methamphetamine dependence as well as in patients with schizophrenia.[7,12] These findings also illustrate the clinical importance of identifying risk factors for suicide attempt among patients with methamphetamine dependence. Additionally, there is emerging literature[31] indicating that antidepressants may produce agitation that potentially increases the risk of suicide. In the present study, 18 of 90 subjects (20%) had agitated behavior after their latest discharge. However, no significant difference regarding the proportion of agitation was found in those with antidepressant use and those without its use (12.5% vs 20.7%, respectively; $P = 1.00$, Fisher exact test). Therefore, it was not an issue for the present study.

In addition to risk factors, we found that financial independence was a strong protective factor for suicide mortality among patients with methamphetamine dependence. It should be pointed out that, although most of the cases and controls in this study were employed at some time during their lifetime, few were actively employed shortly before their latest admission. Thus, financial independence rather than employment appears to be a more useful marker for predicting suicide among subjects who tend to be unemployed due to their illness. This fact may also explain the failure of previous studies[12,32,33] among major psychiatric patients to find association between unemployment and suicide. Our results suggest that the financial condition of patients with methamphetamine dependence should be evaluated closely, and active vocational programs following patient detoxification treatment are needed for the prevention of suicide mortality.

Limitations

This study is limited in several ways. First, our use of chart review instead of face-to-face interviews might have led to underestimation of the prevalence of psychotic symptoms.

Nevertheless, the prevalence of psychotic symptoms in both cases (89.5%) and controls (76.3%) is comparable to the corresponding figure in a previous study[10] of methamphetamine-dependent inpatients using a diagnostic interview scale (85.0%). These comparisons indicate that the underestimation of psychotic symptoms in our study is very likely minimal. Second, although this study employed a national identification system that allows tracking of each suicide event, we might still have missed patients who died of suicide but whose deaths were misclassified as due to other causes, eg, "accidental death," which is the most common term used to avoid the potential stigma associated with suicide.[34] Third, the adjusted risk ratio of anxiety with clinical attention was quite high (2.94) in the final model, but it had an insignificant *P* value, which could be due to the fair sample size in the present study. This reminds us that anxiety with clinical attention could be a potential risk factor for suicide among methamphetamine dependents during the recovery stage, particularly since anxiety is implicated as a suicidality factor among psychiatric patients.[35] In the future, a larger sample is warranted to confirm anxiety as a risk factor for suicide. Finally, the proportion of patients who were lost to follow-up after the latest admission was relatively high (21.1%). However, the resulting bias, if existing, would be more likely to cause underestimation of the risk ratios for correlates (ie, toward the null) since there was no difference in this proportion between cases and controls.

Implications

In terms of the extent of the influence on suicide among patients with methamphetamine dependence attributed to the correlates identified in this study, both the attributable and protective fractions were greater than 60%, regardless of the model used for the estimation. These findings imply that either enhancing the protective factor (financial independence) or diminishing the risk factors (visual hallucination in the acute stage as well as nonfatal attempted suicide and depressive syndrome in the recovery stage) could help prevent the subsequent suicide mortality. This study highlights the importance of clinicians' gathering information regarding the identified risk factors carefully, as well as detecting the high-risk patients earlier, to prevent suicides among these patients. Furthermore, implementing vocational programs after patient detoxification treatment is also important for the prevention of suicide.

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Author contributions: Drs Kuo, C. C. Chen, and W. J. Chen conceived and designed the study; Ms Chang acquired the data; Mr Liao performed the statistical analysis; Drs Tsai and Lin provided administrative and material support; Dr Kuo drafted the manuscript; Drs Conwell and W. J. Chen made critical revisions to the manuscript for important intellectual content; and Drs C. C. Chen and W. J. Chen supervised the study and contributed equally to this article.

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